Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 5-7, 9-12, and 14-23 stand rejected for being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter regarded by Applicants as the invention. Specifically, claims 5 and 6 recite fragments of the erythropoietin protein ("EPO") based on the numbering of the amino acid positions of natural EPO. The specification teaches that natural EPO is 166 amino acids ("a.a.") in length. The Office indicates that the art allegedly teaches that human EPO is 193 a.a. and rat EPO is 192 a.a. long. In light of this observation, the Office asserts that the numbering of the a.a. will be considered as having an additional 27 a.a. placing residue 166 at residue 193 of human EPO. Applicants respectfully traverse the Office's rejection for the following reason.

Applicants assert that the additional 27 a.a. comprise the signal peptide which is a part of the EPO precursor protein as discussed at page 1, lines 20-21 of the specification. Because the signal peptide is cleaved off during EPO protein maturation, it is not part of the mature EPO protein sequence. In support of this assertion, Applicants present two explanations that reconcile the Office's observation with the instant specification and claimed invention.

First, Applicants refer to the specification and the Office's GenBank listings (Accession Nos. NP 000790 and NP 058697) which, when taken together, demonstrate that the initial 26 to 27 a.a. in the GenBank rat and human EPO sequences constitute a signal peptide. Specifically, as set forth on pages 3 (line 30) and 5 (line 2) of the specification, the mature EPO protein sequence begins with a.a. residues "APPRLIC ." In the GenBank human EPO protein (Accession No. NP 000790), which is actually the precursor protein, the "APPRLIC " sequence

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

begins at a.a. position 28. Given that the total length of this human EPO protein is 193 a.a., cleavage of the first 27 a.a. would result in a protein 166 a.a. long, which is consistent with the EPO protein length disclosed in the specification. Likewise, in the GenBank rat EPO protein (Accession No. NP 058697), the "APPRLIC" sequence begins at a.a. position 27. Given that this sequence is 192 a.a. long, cleavage of the first 26 a.a. would also result in a mature EPO protein of 166 amino acids. Thus, both listings are consistent with the specification's disclosure of a natural EPO protein 166 a.a. long.

Second, Applicants submit two abstracts obtained from the Medline database (Lin et al. *PNAS-USA* 82:7580-84 (1985); Nagao et al. *Biochim. Biophy.s Acta.* 1117:99-102 (1992)). These abstracts are taken from references recited in each of the Office's GenBank listings and thus refer to the exact rat and human EPO sequences disclosed in the listings. Both abstracts clearly indicate that the mature EPO protein is 166 a.a. in length. Further, the Lin et al. abstract expressly indicates that the 193 a.a. GenBank human EPO sequence includes a 27 a.a. signal peptide.

In sum, Applicants contend that the Office's GenBank listings are consistent with a mature EPO protein length of 166 a.a. as disclosed in the instant specification. Thus, the Office's proposed renumbering of the specification's EPO sequence is unnecessary, as there is no discrepancy between the specification's disclosure of 166 a.a. and these art-recognized sequences given that the latter sequences include a signal peptide. Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Rejection Under 35 U.S.C. § 102(b)

Claims 5, 12, and 23 stand rejected as allegedly anticipated by Sytkowski et al. (U.S. Pat. No. 4,590,168; "Sytkowski"). Specifically, the Office notes that claim 5 is drawn in part to a method of generating epitope-specific EPO antibodies comprising immunizing an animal with the peptide consisting "essentially" of a.a. 7-22 (P4/1) and isolating the epitope-specific antibody. According to the Office, Sytkowski discloses in claim 12 a method of generating an antibody to the peptide APPRLINDSRVLERYLLEAKEAEKIT which consists "essentially" of the instant P4/1 peptide. Furthermore, the Office contends that Sytkowski also discloses a diagnostic kit containing a peptide consisting of EPO a.a. 156-166. Finally, the Office submits that Sytkowski does not specifically disclose that the antibody generated to the above-mentioned binds to the EPO receptor but that this peptide consists "essentially" of the P4/1 peptide. Thus, according to the Office, Sytkowski's antibody will bind the EPO receptor. Applicants traverse this rejection by addressing this rejection according to each claim rejected.

First, in asserting that claim 5 is anticipated by Sytkowski, the Office specifically refers to the instant P4/1 peptide. Applicants note that this peptide is not recited in claim 5. Rather, a related peptide, P4, is recited in the claim. Sytkowski discloses and claims a method of generating antibodies using a peptide of 6 to 26 a.a. that lie within the N-terminal 26 a.a. of the EPO protein. In contrast, instant claim 5 recites the use of a peptide consisting of the N-terminal 35 amino acids. Applicants respectfully assert that for a reference to anticipate a claimed invention, it must disclose all elements of the claimed invention such that each element is identical between the claimed invention and the reference. Sytkowski's peptides and the claimed

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

P4 peptide are not identical and thus fall short of the legal standards for anticipation. Applicants note that the Office's use of the word "essentially" also acknowledges the lack of identity between these peptides. Thus, Sytkowski cannot anticipate claim 5.

Second, the Office rejects claim 12 as allegedly anticipated by Sytkowski. In making this rejection, the Office asserts that Sytkowski discloses a diagnostic kit containing a peptide consisting of EPO a.a. 156-166. Upon thorough review of Sytkowski, Applicants cannot find any such disclosure and request the Office to specifically indicate the location of this alleged disclosure in the reference. Applicants contend that the only peptide disclosed by Sytkowski in the context of a diagnostic kit, or any context, spans a.a. 1-26 of the EPO protein. *See* Sytkowski, claims 13-15. Applicants assert that, for the reason discussed above regarding claim 5, even this disclosure fails to anticipate claim 12 because Sytkowski's peptides are not identical to the P4 peptide.

Third, the Office contends that claim 23 is also anticipated by Sytkowski. In making this rejection, the Office notes that Sytkowski does not specifically disclose that their antibodies bind the EPO receptor. This observation is inapposite to claim 23 because it recites antibodies that bind EPO protein domains that in turn bind to the receptor rather than antibodies that directly bind the EPO receptor. Thus, Applicants respectfully assert that the Office has misinterpreted the meaning of claim 23. Nonetheless, the Office expressly admits that Sytkowski does not disclose this element of claim 23, again demonstrating that Sytkowski fails to anticipate this claim. Moreover, Applicants note that claim 23 is dependent on claim 6, not claim 5. Claim 6 does not recite peptide P4 but does recite peptides P2 and P2/1. As discussed above in the

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

context of claim 12, we find no evidence that Sytkowski discloses the use of a peptide consisting of EPO a.a. 156-166. Furthermore, even if this peptide were disclosed, it is not identical to peptides P2 and P2/1 of the claimed invention.

In conclusion, for the reasons discussed above, the Office's rejection of claims 5, 12, and 23 does not satisfy the legal standards for anticipation. Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(b).

Obviousness-Type Double Patenting

Claims 6, 7, 11, and 17-21 stand rejected for obviousness-type double patenting over claims 1 and 2 of U.S. Patent No. 5,712,370. Applicants request that this rejection be held in abeyance until allowable subject matter has been indicated.

Conclusion

Applicants respectfully request that this Response be entered by the Office, placing claims 5-7, 9-12, and 14-23 in condition for allowance.

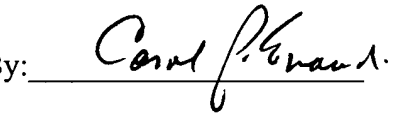
In view of the foregoing remarks, Applicants submit that their claimed invention is not anticipated in view of the prior art reference cited against this application. Applicants therefore respectfully request the entry of this Response, the Office's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Please grant any additional extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: 

Carol P. Einaudi
Reg. No. 32,220

Date: February 5, 2001

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000